ILLUSTRATED GUIDE

For Grading

Eye

Irritation Caused by Hazardous Substances

INTRODUCTION

The Consumer Product Safety Act (CPSA)[1] signed into law by the President on October 27, 1972, established a new independent Federal Regulatory Agency, the Consumer Product Safety Commission (CPSC).

The CPSA is designed (1) to protect the public against unreasonable risks of injury associated with consumer products, (2) to assist consumers in evaluating the comparative safety of consumer products, (3) to develop uniform safety standards for consumer products, (4) to minimize conflicting State and local regulations, and (5) to promote research and investigation into the causes and prevention of product related deaths, illnesses, and injuries.

With the enactment of the CPSA, the functions of the Secretary of Health, Education, and Welfare under the Federal Hazardous Substances Act (FHSA)[2] were transferred to the CPSC. The FHSA Regulations, 16 CFR 1500.3(c)(4), state that the definition of "irritant" in Section 2(j) of the FHSA is supplemented by the following: "'Irritant' includes...substances irritant to the eye...'Eye Irritant' means a substance that human experience data indicate is an irritant to the eye and/or means a substance for which a positive test is obtained when tested by the method described in Section 1500.42". A copy of 16 CFR 1500.42, Test for eye irritants, is included in this guide. (Note: Before the responsibility for the FHSA was transferred to the CPSC, this method was found at 21 CFR 191.12.) This method for evaluating eye irritation, originally referred to as the Draize Technique[3] was initially published in 1944 as a test for evaluating drugs and cosmetics. In the September 17, 1964 *Federal Register*[4] the method was modified for the purpose of evaluating substances subject to the FHSA. In the April 28,1972 *Federal Register*[5] a proposal to revise the present method was published. This proposal has not been finalized; any future modification of the method will be published in the *Federal Register*.

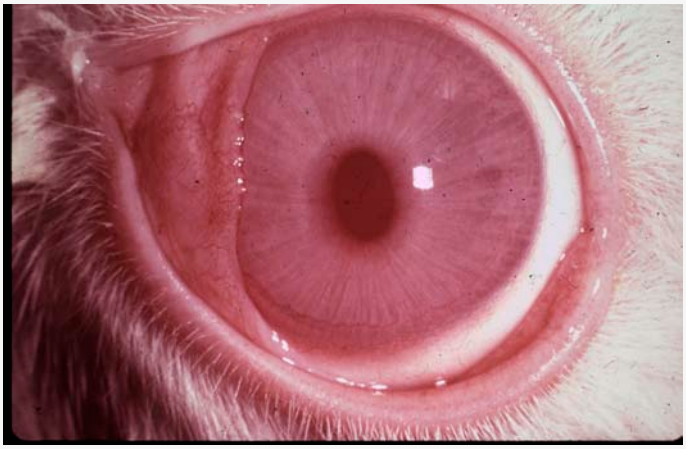
As with any test which relies on subjective interpretation, grading ocular reactions poses a major problem. The purpose of this publication is to assist in training laboratory personnel and other interested persons in evaluating eye injury, and thereby contribute to more uniform interpretations of the results obtained when a substance is tested in accordance with the official method. This guide is intended to be used as a reference tool rather than as an absolute standard.

[1] 15 U.S.C. 2051
[2] 15 U.S.C. 1261
[3] Draize, J.H., Woodard, G., and Calvery, H.O. J.Pharmacol. Exp. Ther., 82, 377-390 (1944)
[4] 29 FR 13009
[5] 37 FR 8534

DESCRIPTION OF SLIDES

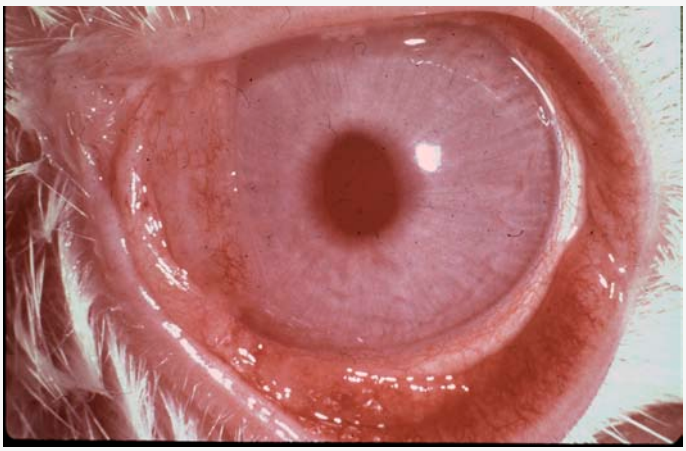
1. Normal Eye
2. Grade 1 Redness
3. Grade 2 Redness
4. Grade 3 Redness
5. Lackluster/Pitting
6. Grade 1 Opacity
7. Grade 2 Opacity
8. Grade 3 Opacity
9. Grade 4 Opacity
10. Grade 1 Iritis
11. Grade 2 Iritis
12. Grade 1 Chemosis
13. Grade 2 Chemosis
14. Grade 3 Chemosis
15. Grade 4 Chemosis
16. Pannus
17. Corneal bulging
18. 48 Hours--Without Fluorescein
19. 48 Hours--With Fluorescein
20. 72 Hours--With Fluorescein (note corneal regeneration)

1. Normal Eye

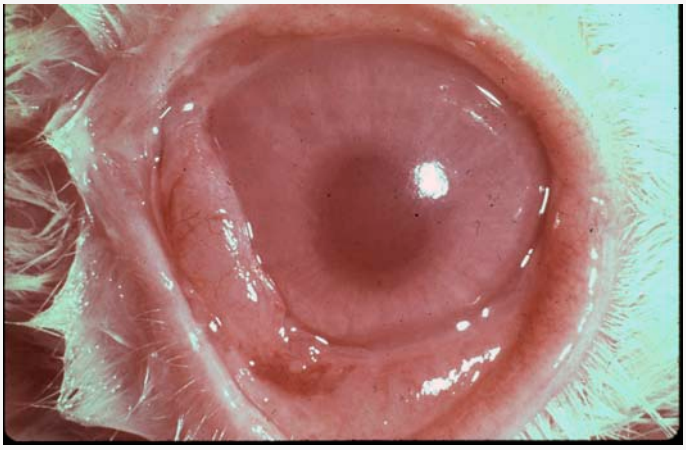


2. Grade 1 Redness

3. Grade 2 Redness

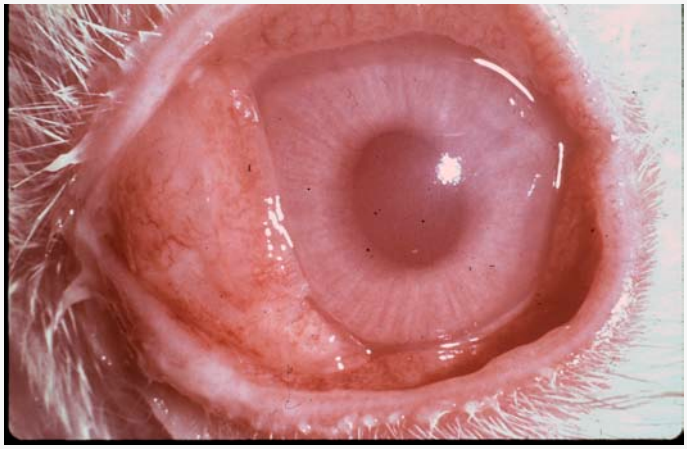


4. Grade 3 Redness

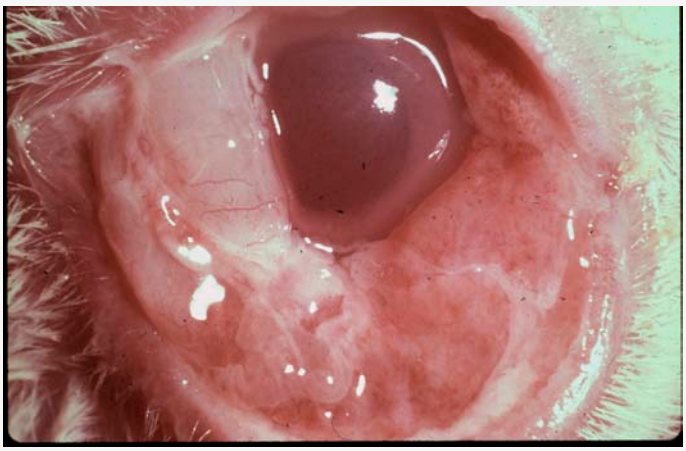


5. Lackluster/Pitting

6. Grade 1 Opacity

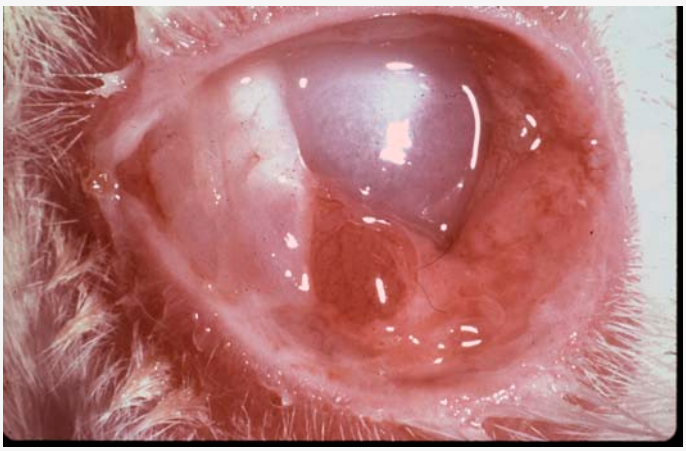


7. Grade 2 Opacity

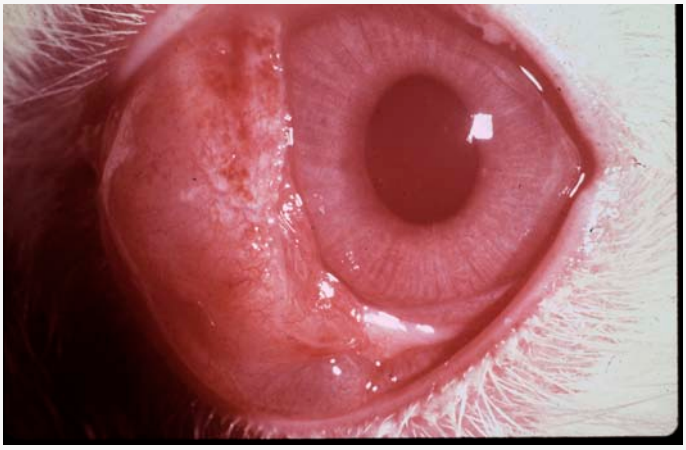


8. Grade 3 Opacity

9. Grade 4 Opacity



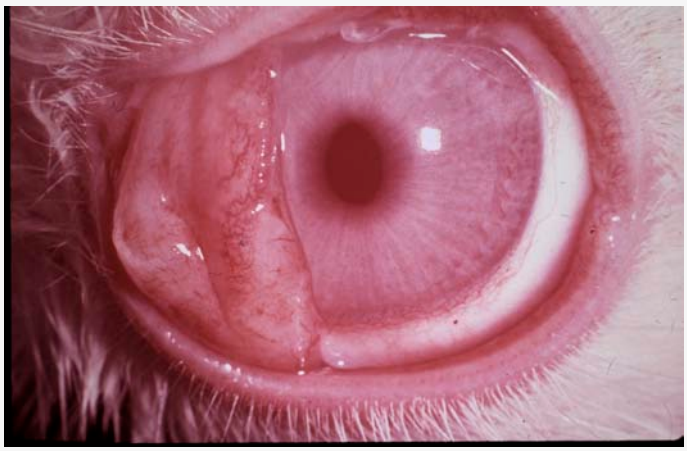
10. Grade 1 Iritis



11. Grade 2 Iritis

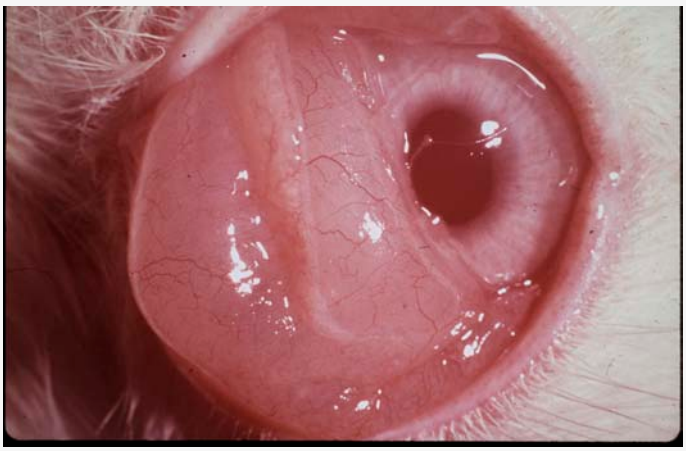
12. Grade 1 Chemosis

13. Grade 2 Chemosis

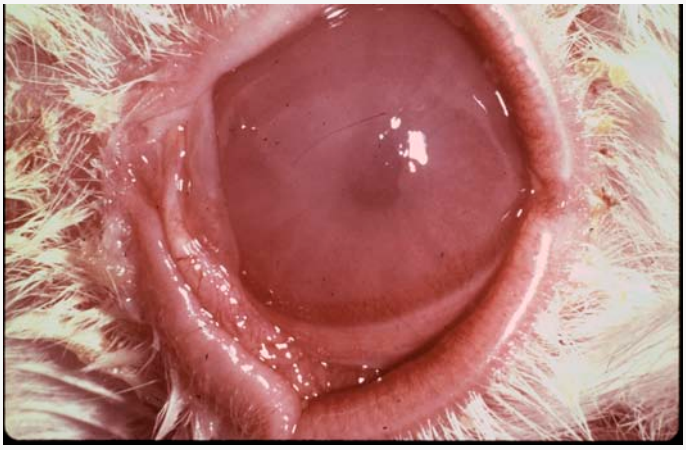


14. Grade 3 Chemosis

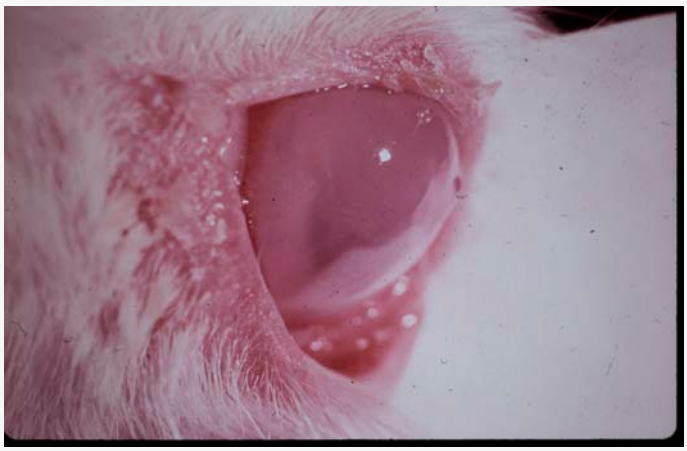
15. Grade 4 Chemosis



16. Pannus



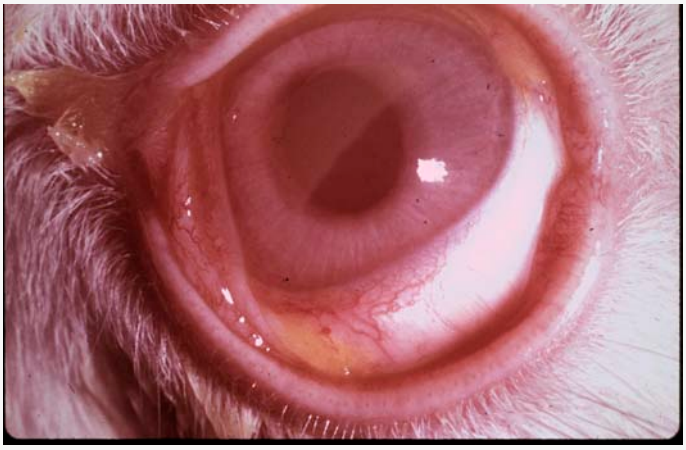
17. Corneal bulging



18. 48 Hours—Without Fluorescein

19. 48 Hours—With Fluorescein

20. 72 Hours—With Fluorescein (note corneal regeneration)



GRADING

When grading by the official method, each structure of the eye is considered independently. Damage is scored on the basis of the intensity of response of the most severely affected portion; the area of involvement is not taken into consideration. However, for purposes of illustration, the plates and slides in this guide are not necessarily graded on the most severely affected portion.

For completeness in judging the severity of the reaction caused by the test material, corneal lesions such as necrosis (death of tissue), pannus (subepithelial proliferation, pigmentation and accompanying vascularization of the cornea), and corneal bulging should be noted. If any of these conditions are observed during the test period, severe ocular damage is indicated. In slide 8 note the necrosis of the nictitating membrane. Pannus and corneal bulging are illustrated in slides 16 and 17 respectively.

Although not part of the official method, grading the eyes at 1 hour and 7, 14, & 21 days after instillation of the test substance is often helpful in judging the severity of the reaction. (On Plate 6 note the 4 chemosis at 1 hour and 4 opacity at 7 days which would not have been observed during the official test period.)

Slide 5 illustrates two commonly observed injuries which are not considered positive reactions: lackluster (dulling of the cornea less than a grade 1 opacity) and pitting (fine stippling effect of the cornea).

As described in 16 CFR 1500.42, an optional method for reading reactions is to place one drop of fluorescein sodium ophthalmic solution (U.S.P. or equivalent) in the eye. After flushing out the excess fluorescein with sodium chloride solution (U.S.P. or equivalent), injured areas of the cornea appear yellow. This is best visualized in a darkened room under ultraviolet illumination. Plate 3 and slides 19 and 20 illustrate ocular damage as evidenced by fluorescein staining. Slides 18 through 20 illustrate damage at 48 hours with and without fluorescein staining, and subsequent corneal regeneration at 72 hours indicated by a smaller stained area.

§1500.42 Test for eye irritants.

(a)(1) Six albino rabbits are used for each test substance. Animal facilities for such procedures shall be so designed and maintained as to exclude sawdust, wood chips, or other extraneous materials that might produce eye irritation. Both eyes of each animal in the test group shall be examined before testing, and only those animals without eye defects or irritation shall be used. The animal is held firmly but gently until quiet. The test material is placed in one eye of each animal by gently pulling the lower lid away from the eyeball to form a cup into which the test substance is dropped. The lids are then gently held together for one second and the animal is released. The other eye, remaining untreated, serves as a control. For testing liquids, 0.1 milliliter is used. For solids or pastes 100 milligrams of the test substance is used, except that for substances in flake, granule, powder, or other particulate form the amount that has a volume of 0.1 milliliter (after compacting as much as possible without crushing or altering the individual particles, such as by tapping the measuring container) shall be used whenever this volume weighs less than 100 milligrams. In such a case, the weight of the 0.1 milliliter test dose should be recorded. The eyes are not washed following instillation of test material except as noted below.

(2) The eyes are examined and the grade of ocular reaction is recorded at 24, 48, and 72 hours. Reading of reactions is facilitated by use of a binocular loupe, hand slit-lamp, or other expert means. After the recording of observations at 24 hours, any or all eyes may be further examined after applying fluorescein. For this optional test, one drop of fluorescein sodium ophthalmic solution U.S.P. or equivalent is dropped directly on the cornea. After flushing out the excess fluorescein with sodium chloride solution U.S.P. or equivalent, injured areas of the cornea appear yellow; this is best visualized in a darkened room under ultraviolet illumination. Any or all eyes may be washed with sodium chloride solution U.S.P. or equivalent after the 24 hour reading.

(b)(1) An animal shall be considered as exhibiting a positive reaction if the test substance produces at any of the readings ulceration of the cornea (other than a fine stippling), or opacity of the cornea (other than a slight dulling of the normal luster), or inflammation of the iris (other than slight deepening of the folds (or rugae) or a slight circumcorneal injection of the blood vessels), or if such substance produces in the conjunctivae (excluding the cornea and iris) an obvious swelling with partial eversion of the lids or a diffuse crimson-red with individual vessels not easily discernible.

(2) The test shall be considered positive if four or more of the animals in the test group exhibit a positive reaction. If only one animal exhibits a positive reaction, the test shall be regarded as negative. If two or three animals exhibit a positive reaction, the test is repeated using a different group of six animals. The second test shall be considered positive if three or more of the animals exhibit a positive reaction. If only one or two animals in the second test exhibit a positive reaction, the test shall be repeated with a different group of six animals. Should a third test be needed, the substance will be regarded as an irritant if any animal exhibits a positive response.

GRADES FOR OCULAR LESIONS

Cornea

No ulceration or opacity	0
Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible	(1)*
Easily discernible translucent areas, details of iris slightly obscured	2
Nacreous areas, no details of iris visible, size of pupil barely discernible	3
Complete corneal opacity, iris not discernible	4

Iris

Normal	0
Markedly deepened folds, congestion, swelling, moderate circumcorneal injection (any of these or combination of any thereof), iris still reacting to light (sluggish reaction is positive)	(1)*
No reaction to light, hemorrhage, gross destruction (any or all of these)	2

Conjunctivae

Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	
Vessels normal	0
Some vessels definitely injected	1
Diffuse, crimson red, individual vessels not easily discernible	(2)*
Diffuse beefy red	3
Chemosis	
No swelling	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of lids	(2)*
Swelling with lids about half closed	3
Swelling with lids more than half closed	4

*** Bracketed figures indicate lowest grades considered positive under the Federal Hazardous Substances Act Regulations at 16 CFR 1500.42.**

DESCRIPTION OF PLATES

Plate 1 - A normal eye and grades 1 through 3 redness.

Plate 2 - Grades 1 through 4 corneal opacity.

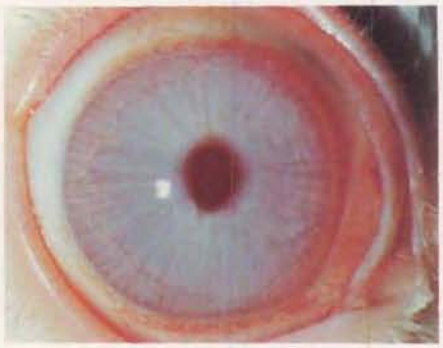
Plate 3 - The same eyes as in Plate 2 stained with fluorescein and shown under ultraviolet illumination:

Plate 4 - Grades 1 and 2 iritis.

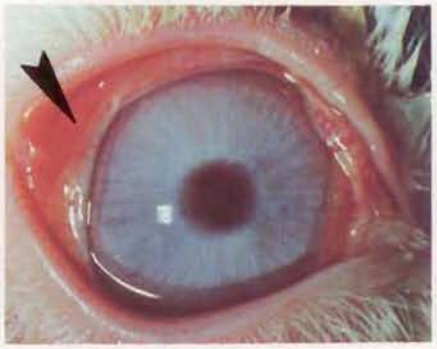
Plate 5 - Grades 1 through 4 chemosis.

Plate 6 - The same eye prior to instillation through 1 hour, 24 hours, 48 hours, 72 hours, and 7 days after product instillation. Each eye is scored for redness, opacity, iritis, and chemosis.

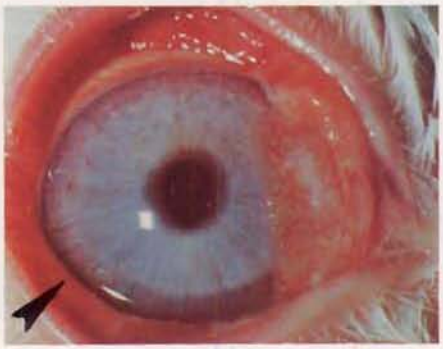
PLATE 1



Normal Eye



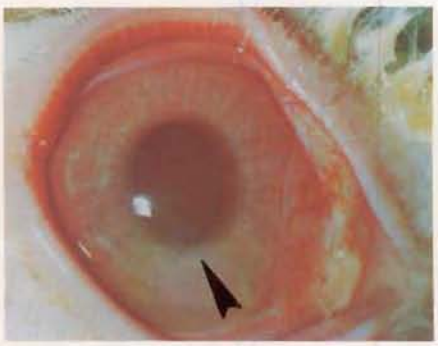
1 Redness



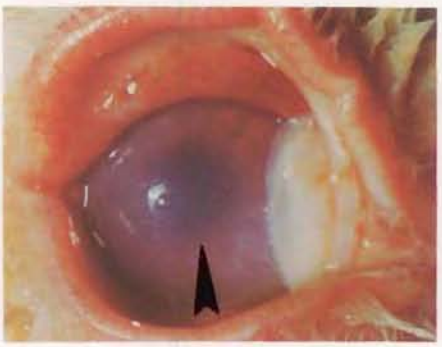
2 Redness

3 Redness

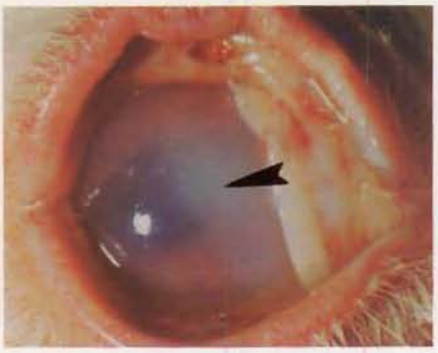
PLATE 2



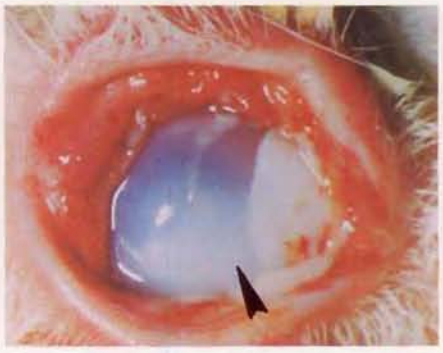
1 Opacity



2 Opacity

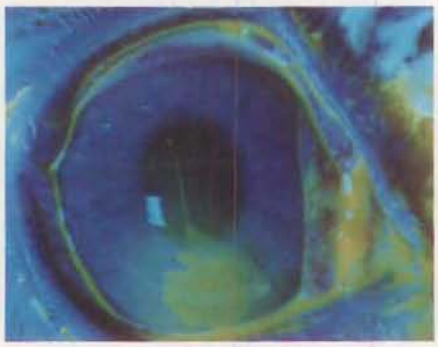


3 Opacity

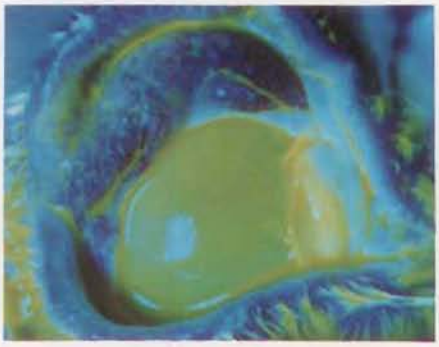


4 Opacity

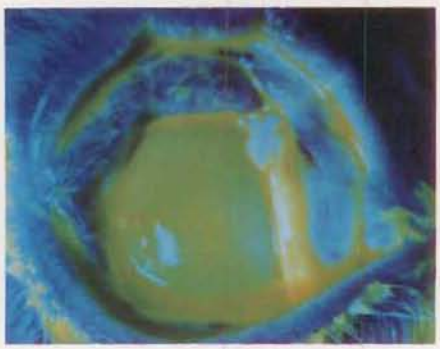
PLATE 3



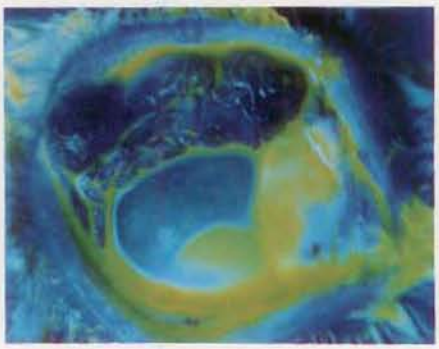
1 Opacity



2 Opacity

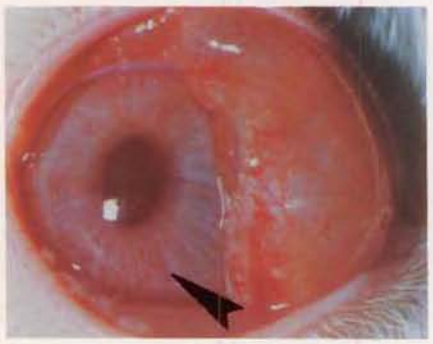


3 Opacity

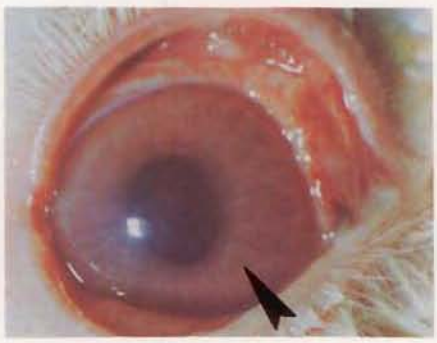


4 Opacity

PLATE 4

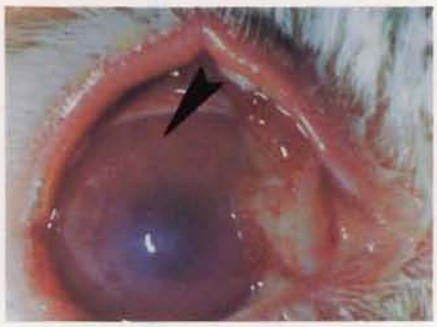


1 Iritis



1 Iritis

2 Iritis



2 Iritis

PLATE 5

1 Chemosis

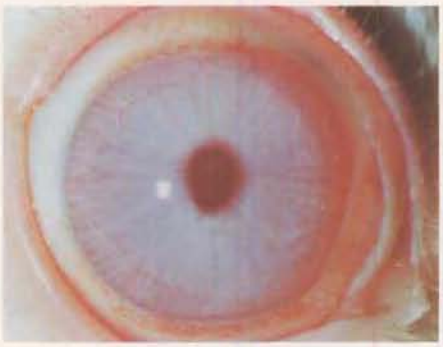
2 Chemosis

3 Chemosis

4 Chemosis

These photographs may not accurately represent chemosis because the eyes have been held open to show other aspects of irritation.

PLATE 6



Normal Eye

1 Hour

2-3 Redness
1 Iritis
> 2 Opacity
4 Chemosis

24 Hours

3 Redness
2 Iritis
1 Opacity
> 3 Chemosis

48 Hours

3 Redness
2 Iritis
> 1 Opacity
3 Chemosis

72 Hours

3 Redness
2 Iritis
> 1 Opacity
> 2 Chemosis

7 Days

3 Redness
2 Iritis
4 Opacity
2 Chemosis

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